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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Tsutomu Ishihara

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EXAMINER

DICKINSON, PAUL W

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/596,828	Applicant(s) ISHIHARA ET AL.	
	Examiner PAUL DICKINSON	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,5-22 and 24-27 is/are pending in the application.
- 4a) Of the above claim(s) 20-22 and 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,3,5-19 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments, filed 9/12/2008, have been fully considered but they are not deemed to be fully persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Claim Rejections - 35 USC § 102

The rejection of claims 2, 6, and 8-10 under 35 U.S.C. 102(b) as being anticipated by WO '298 is maintained.

Applicant argues that the nanoparticles of WO '298 are composite particles that require an organic polymer among other components. In contrast, the instant invention does not have these components.

Applicant's arguments have been fully considered but are not found persuasive. The claimed invention uses open terminology to describe the contents of the nanoparticles (i.e. containing) and are open to such components.

The rejection of claims 3 and 11-18 under 35 U.S.C. 102(b) as being anticipated by WO 03033592 (WO '592) is maintained.

Applicant argues that WO '592 relates to a polymeric micelle composition comprising an amphiphilic block copolymer composed of a hydrophilic block and a

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hydrophobic block. There are no block polymers in the nanoparticles of the present invention.

Applicant's arguments have been fully considered but are not found persuasive. The claimed invention uses open terminology to describe the contents of the nanoparticles (i.e. containing) and are open to such components.

Claim Rejections - 35 USC § 103

The rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over WO 03033592 (WO '592) in view of US 3701745 ('745) is maintained.

Applicant repeats the arguments made given for the rejection of claims 3 and 11-18 under 35 U.S.C. 102(b) as being anticipated by WO '592. Furthermore, Applicant argues that one is not likely to look at '745 as this patent is drawn to coating dispersions used to coat plastic film and paper products, and such a composition would not likely be safe or pharmaceutically acceptable for a drug delivery system.

Applicant's arguments have been fully considered but are not found persuasive. The Examiner addressed Applicant's arguments regarding WO '592 above. In response to Applicant's argument that '745 is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In the present case, '745 gives a general teaching of polymers that may be used as components in micelles.

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Furthermore, '745 does teach that oleic acid is useful in micelle chemistry. Specifically, it states "In general, those non-ionic surfactants which lower surface tension of water to not less than about 40 dynes/cm, and preferably to not less than 42.5 dynes/cm, are operable. These include polyoxyalkylene derivatives of various compounds such as those of octylphenol... or nonylphenyl, of sorbitan esters such as those of lauric acid, palmitic acid, stearic acid and oleic acid... A sufficient amount of the non-ionic surfactant is included in the reaction medium to produce micelles of the polymerizing monomers." Thus, oleic acid may be used as a component in micelles. The Examiner maintains that it would be obvious to substitute the carboxyl terminated lactic acid of WO '592 for oleic acid, as these compounds are functional equivalents.

The rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over WO 9941298 (WO '298) in view of US 6159381 ('381) is maintained.

Applicant argues, in addition to the arguments presented above regarding WO '298, that one is unlikely to look to the water paper treatment art, which is the subject area of US '381.

Applicant's arguments have been fully considered but are not found persuasive. As stated above, the claimed invention uses open terminology to describe the contents of the nanoparticles (i.e. containing) is open to such components. Regarding the reliance of '381 to support the rejection, as stated above, a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied

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upon as a basis for rejection of the claimed invention. In the present case, '381 was relied on for the teaching that carbonates are used to cause alkaline earth metal salts to precipitate from aqueous solutions. The Examiner maintains that it would be obvious to substitute a carbonate salt for the sodium hydroxide of WO '298, as these compounds are functional equivalents.

The rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over WO 9941298 (WO '298) is maintained.

Applicant argues that the nanoparticles of WO '298 are composite particles that require an organic polymer among other components. In contrast, the instant invention does not have these components.

Applicant's arguments have been fully considered but are not found persuasive. The claimed invention uses open terminology to describe the contents of the nanoparticles (i.e. containing) and are open to such components.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24 recites "mixing a fat-soluble or fat-solubilized water-

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soluble drug and a C₆-C₂₄ fatty acid or its salt in a ratio of about 1:30 to 1:0.03". It is unclear if this is a respective ratio (that this is the "fat-soluble or fat solubilized water-soluble drug" to "C₆-C₂₄ fatty acid or its salt" ratio or the "C₆-C₂₄ fatty acid or its salt" to "fat-soluble or fat solubilized water-soluble drug" ratio. The weight ratio ranges "0.3 to 0.01", "5 to 0.01", and "1.0 to 0.05 " are unclear for similar reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3, 11-12, 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9941298 (hereafter WO '298; US 6685966 ('966) is an English equivalent and will be referenced hereafter). WO '298 discloses drug-containing nanoparticles provided by causing primary nanoparticles containing a hydrophobic active material (fat-soluble drug) to act with alkaline earth metal salts (bivalent metal salts) to give secondary nanoparticles, and causing bases such as sodium hydroxide or potassium hydroxide (a monovalent basic salt) to act with the secondary particles (see

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'966: col 1, lines 51-61; col 4, lines 39-65; col 7, lines 34-35; Examples 1-2). The nanoparticles are solubilized with at least one emulsifiers such as C₆-C₂₄ fatty acids and other surfactants (see col 5, lines 13-29). The particles have a diameter of 0.21 microns (210 nm) (Example 1). The Examiner is giving "200 nm" in instant claim 19 only one significant figure, and is thereby interpreting 210 nm to be encompassed by 200 nm. The exemplified nanoparticles are prepared by causing the primary particles to act with calcium chloride to give secondary nanoparticles and causing sodium hydroxide to act with the secondary nanoparticles (see '996: Example 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9941298 (hereafter WO '298; US 6685966 ('966) is an English equivalent and will be referenced hereafter). WO '298 discloses drug-containing nanoparticles provided by

1) mixing a fat-soluble drug with a polymer to create initial nanoparticles

2) mixing the initial nanoparticles with one or more emulsifiers such as C₆-C₂₄ fatty acids and surfactants such as polyethoxylated alcohol to make primary nanoparticles;

3) mixing at least one alkaline earth metal salt (bivalent metal salt) with the primary nanoparticles to make secondary nanoparticles, and

4) mixing sodium or potassium hydroxide (a monovalent basic salt) with the secondary nanoparticles to make tertiary nanoparticles (see '966: col 1, lines 51-61; col 4, lines 39-65; col 7, lines 34-35; Examples 1-2).

The drug:C₆-C₂₄ fatty acid weight ratio may range from 33:1 to 1.1:1 (see col 5, lines 30-32; Examples 1-2; 33:1 is calculated from 41/1.25 and 1.1:1 is calculated from 41/37.5, where 41 is the weight of the drug in grams calculated from 145(500/(500 + 1250)), where 1.25 is calculated from (1250)(0.001), and where 37.5 is calculated from

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(1250)(0.03) where 1250 is the weight in grams of the polymer from Examples 1-2).

The surfactant:fatty acid weight ratio may range from 1.7:1 to 0.57:1 (1.7:1 calculated from 2.144/1.25 and 0.57:1 calculated from 2.144/37.5 where 2.144 is the weight in grams of polyethoxylated alcohol and 1.25 and 37.5 are calculated as above). The alkaline earth metal salt:drug weight ratio is 0.05 (calculated from 2.114/41 where 41 is the weight in grams of the drug). Enough sodium or potassium hydroxide is added to bring the mixture to a pH of 8-11 (see col 8, lines 4-8; Example 2).

Instant claim 27 is a product-by-process claim. “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP § 2113. The claimed tertiary nanoparticles are prepared by a process comprising the steps of a), b), and c). Although the nanoparticles of WO '398 further comprise an organic polymer, such a component is not excluded by the claimed invention.

WO '398 fails to recite the “basic salt” to “monovalent to trivalent basic salt” weight range of 1.0 to 0.05.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to optimize the amount of sodium or potassium hydroxide to

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find the instantly claimed range, as WO '298 teaches adding an appropriate amount of the salt to reach a pH of 8-11. See MPEP § 2144.05, II.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **PAUL DICKINSON** whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

December 19, 2008